REMARKS

Claims 17-35 are pending. In a first substantive Office Action mailed July 12, 2006, the Examiner has raised several issues, which are set forth by number in the order they are addressed herein:

1) Claims 17-35 stand rejected under 35 U.S.C. § 112 second paragraph, as allegedly being indefinite;
2) Claims 26-34 stand rejected under 35 U.S.C. § 112 first paragraph, as allegedly lacking enablement;
3) Claims 17-21 and 23-35 stand rejected under 35 U.S.C. § 112 first paragraph, as allegedly lacking enablement;
4) Claims 17-19, 23 and 24 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lombillo et al., J Cell Biol, 128:107-115, 1995 (Lombillo);
5) Claims 17-19, 24 and 25 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Thrower et al., EMBO J, 14:918-926, 1995 (Thrower);
6) Claims 17 and 20-22 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Lombillo in view of Duesbery et al., Proc Natl Acad Sci USA, 94:9165-9170, 1997 (Duesbery); and
7) Claims 17 and 35 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Lombillo or Thrower in view of U.S. Patent No. 5,759,795 to Jubin (Jubin).

Applicants hereby amend Claims 17, 18, 21, 22 and 27, cancel Claims 23, 26 and 30-34, and add new Claims 43-54, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments. Applicants reserve the right to prosecute the original, similar, or broader claims in one or more future application(s). The amendments do not introduce new matter.

1) The Claims Are Definite

The Examiner has rejected Claims 17-35 under 35 U.S.C. § 112 second paragraph, as allegedly being indefinite. The Examiner indicates that Claim 17 is indefinite for not defining the acronym "CENP-E" in its first occurrence in the claims. Although Applicants believe the claims as filed are definite, Applicants have amended Claim 17 in order to further the

prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Applicants have amended Claim 17 to recite "centromere-associated protein E (CENP-E)." Support for this amendment can be found in the teaching that "'CENP-E' refers to centromere-associated protein, which is a member of the kinesin superfamily of microtubule motor proteins" (Specification, paragraph [0072]). As the amended claims are definite, Applicants respectfully request that this rejection be withdrawn.

2 & 3) The Claims Are Enabled

The Examiner has rejected Claims 26-34 under 35 U.S.C. § 112 first paragraph, as allegedly lacking enablement for being drawn to identifying lead therapeutic, lead bioagricultural, or lead diagnostic compounds without teaching how to use CENP-E modulators for these purposes (Office Action, page 2). Although Applicants respectfully disagree, Applicants have amended Claim 27 to depend upon Claim 17, and have canceled Claims 26 and 30-34 in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s).

The Examiner has also rejected Claims 17-21 and 23-35 under 35 U.S.C. § 112 first paragraph, as allegedly lacking enablement for being drawn to "identifying candidate agents that modulate any and all proteins characterized only by the term 'CENP-E'" (Office Action, page 4). Although Applicants respectfully disagree, Applicants have amended Claims 17 and 21, and entered new Claims 43-54, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Applicants have amended Claims 17 and 21 to recite that CENP-E comprises a motor domain corresponding to or as set forth as amino acids 1-324 of SEQ ID NO:1, respectively. Similarly, new Claims 43 and 44-54 recite that biologically active CENP-E has plus end-directed microtubule motor activity and comprises an amino acid sequence having at least 70% or at least 80% sequence identity with amino acids 1-324 of SEQ ID NO:1. Support for these amendments can be found for instance in the disclosure that "[w]ithin the N-terminal

globular domains of both hCENP-E and XCENP-E there is a domain of ~324 amino acids corresponding to the kinesin like motor domain" (Specification, paragraph [0028]). Further support can be found in, for example, original Claim 8 and pending Claim 17, which recite that CENP-E "has an amino acid sequence having greater than 70% sequence identity with *Xenopus* CENP-E (XCENP-E) motor domain of SEQ ID NO:1" and that CENP-E activity comprises "plus end-directed microtubule motor activity" respectively. Additional support can be found in the summary, which teaches that in some embodiments CENP-E has at least 80% acid sequence identity to a Xenopus CENP-E core motor domain (Specification, paragraph [0014]). Applicants believe the claim amendments and cancellations obviate the enablement rejections and therefore respectfully request that these rejections be withdrawn.

4) The Claims Are Novel Over Lombillo

The Examiner has rejected Claims 17-19, 23 and 24 under 35 U.S.C. § 102(b) as allegedly anticipated by Lombillo et al., J Cell Biol, 128:107-115, 1995 (Lombillo). The Examiner states that

> Lombillo teaches a method for identifying antibodies that modulate CENP-E dependent microtubule depolymerization-driven chromosome motion (which reads on "microtubules motor activity) on page 108 and page 111-112, bridging paragraph. Thus, Lombillo teaches methods that are the same as claimed (Office Action, page 7).

Applicants respectfully disagree. Nonetheless, Applicants have amended Claims 17 and 18, canceled Claim 23, and added new Claims 43-54, in order to further the prosecution of the present application and Applicants' business interests, yet without acquiescing to the Examiner's arguments, and while reserving the right to prosecute the original, similar, or broader claims in one or more future application(s). In particular, Applicants have amended Claim 17 to recite "wherein the CENP-E activity comprises plus-end directed microtubule motor activity" and by inclusion of the step of "providing a substantially purified biologically active CENP-E." Claim 18 has been amended to recite "wherein said CENP-E is a recombinant protein." Support for these amendments can be found in original Claim 23, now canceled, and throughout the application as filed. For instance, Applicants teach that

> [a] protein that is the predominant species present in a preparation is substantially purified. ... The term "purified" denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Particularly, it means that the nucleic acid or protein is at least 85% pure, more preferably at least 95% pure, and most preferably at least 99% pure (Specification, paragraph [0040].

Further support can be found but is not limited to Section IV of the Description directed to methods for purification of CENP-E, including purification from recombinant bacteria (Specification, paragraphs [0104]-[0120]).

In contrast to the pending claims reciting substantially purified biologically active CENP-E, the methods of Lombillo employ native CENP-E contained in crude chromosomal preparations or ATP-extracted microtubule-associated protein preparations (Lombillo, Figure 6 and page 111). Additionally, Lombillo does not teach that CENP-E possesses plus end-directed microtubule motor activity as recited in the claimed methods. Rather Lombillo simply asserts that some anti-CENP-E antibodies reduced chromosome movement, without providing any teaching regarding whether this movement involved plus end-directed or minus-end directed microtubule motor activity. Also, the methods of Lombillo employ hamster CENP-E and human CENP-E, which are distinct from the frog CENP-E and frog-like CENP-E (e.g., at least 80% sequence identity with amino acids 1-324 of SEQ ID NO:1) required by Claims 20-22 and new Claims 44-54. As the amended claim set is clearly distinct from the teaching of Lombillo, Applicants respectfully request that this rejection be withdrawn.

5) The Claims Are Novel Over Thrower

The Examiner has rejected Claims 17-19, 24 and 25 under 35 U.S.C. § 102(b) as allegedly anticipated by Thrower et al., EMBO J, 14:918-926, 1995 (Thrower). The Examiner states that

> Thrower teaches a method for determining nucleotide specificity and inhibitor specificity of microtubule movement due to human CENP-E in a D-100 mitotic extract (see 924-925 and page 920). Thus, Thrower teaches methods that are the same as that claimed (Office action, page 8).

Applicants respectfully disagree. Nonetheless, as described above in Section 4, Applicants have amended Claim 17 to recite "wherein the CENP-E activity comprises plus-end directed microtubule motor activity" and by inclusion of the step of "providing a substantially purified

biologically active CENP-E." Moreover Applicants have amended Claim 18 to recite "wherein said CENP-E is a recombinant protein."

Importantly, Thrower fails to teach that CENP-E possesses plus end-directed microtubule motor activity as recited by the amended claims. Rather Thrower discloses that CENP-E possesses minus end-directed microtubule motor activity (Thrower, title, abstract, and page 919 among other locations), indicating that the motor analyzed by Thrower is distinct from CENP-E of the present invention. Additionally in contrast to the pending claims requiring substantially purified biologically active CENP-E, the methods of Thrower employ native CENP-E contained in S-100 HeLa cell extracts, D100 fractions and microtubule affinity purified protein preparations (Thrower, pages 924 and 925). Moreover, the methods of Thrower employ non-recombinant human CENP-E, which is distinct from the frog CENP-E and frog-like CENP-E (e.g., at least 80% sequence identity with amino acids 1-324 of SEQ ID NO:1) recited in Claims 20-22 and new Claims 44-54, and the recombinant CENP-E recited in Claims 18 and 46. As the amended claim set is clearly distinct from the teachings of Thrower, Applicants respectfully request that this rejection be withdrawn.

6) The Claims Are Non-Obvious Over Lombillo and Duesbery

The Examiner has rejected Claims 17 and 20-22 under 35 U.S.C. § 103(a) as allegedly unpatentable over Lombillo in view of Duesbery et al., Proc Natl Acad Sci USA, 94:9165-9170, 1997 (Duesbery). The Examiner states that the

> specification teaches that an inherent feature of Xenopus CENP-E activity is that it comprises the structure of SEQ ID NO:1 (motor domain). ... Lombillo fails to teach methods where the CENP-E activit[y] is that of Xenopus CENP-E activity. However, Xenopus CENP-E is known in the art as evidenced by the teachings of [Duesbery]. ... Thus, it would have been prima facie obvious to have used the chromosomes isolated from Xenopus eggs as taught by [Duesbery] in the method of Lombillo to make a method that comprised testing for modulators of Xenopus CENP-E activity (Office Action, page 9).

Applicants submit that the Examiner has not established a *prima facie* case of obviousness against the amended claims because the combination of references cited by the Examiner fails to teach all of the elements of the amended claims. In contrast to the pending claims, the combination of Lombillo and Duesbery does not employ substantially purified biologically

active CENP-E, let alone recombinant CENP-E. Additionally, this combination of references does not teach that CENP-E possesses plus end-directed microtubule motor activity as recited by Claim 17 and associated dependent claims. Rather both Lombillo and Duesbery simply assert that some anti-CENP-E antibodies reduced chromosome movement, and that some CENP-E antibodies block the transition form metaphase to anaphase during meiosis I. Neither reference provides any teaching regarding the direction of CENP-E motor activity.

Moreover, while the teachings of Duesbery pertain to XCENP-E, Duesbery fails to provide an amino acid sequence of the motor domain of XCENP-E as recited by Claim 21, let alone an amino acid sequence of full length XCENP-E as recited by Claim 22. "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art" *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). As the XCENP-E amino acid sequence limitations of the claims do not *necessarily* flow from the teachings of Duesbery, these properties are not inherent to this reference (See, MPEP 2112 IV). Moreover, as Lombillo does not remedy the deficiency in the Duesbery disclosure, this combination of references does not make obvious the pending claim set. Thus, Applicants respectfully request that this rejection be withdrawn.

7) The Claims Are Non-Obvious Over Lombillo or Thrower and Jubin

The Examiner has rejected Claims 17 and 35 under 35 U.S.C. § 103(a) as allegedly unpatentable over Lombillo or Thrower in view of U.S. Patent No. 5,759,795 to Jubin (Jubin). The Examiner states that neither

> Lombillo nor Thrower explicit[l]y teach simultaneous screening methods. However, high-throughput screening methods are known in the art as evidenced by the teachings of Jubin for detection of inhibitors of ATPase activity. ... Thus it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Lombillo or Thrower to look for antibodies or nucleotides that inhibited ATP activity in CENP-E using the high throughput screening method of Jubin (Office Action, page 10).

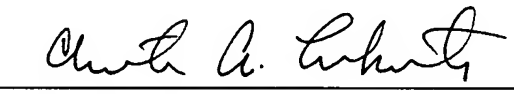
Applicants submit that the Examiner has not established a *prima facie* case of obviousness against the amended claims because the combination of references cited by the Examiner fails to teach all of the elements of the amended claims. In contrast to the pending claims, neither

Lombillo nor Thrower provide methods comprising substantially purified biologically active CENP-E, let alone recombinant CENP-E that possesses plus end-directed microtubule motor activity. As Jubin does not remedy these deficiencies the amended claim set is clearly distinct from and non-obvious in view of Lombillo, Thrower and Jubin. Accordingly, Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

Applicants believe that the arguments and claim amendments set forth above traverse the Examiner's rejections and therefore, request that all grounds for rejection be withdrawn. However, should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect.

Dated: December 8, 2006

By: 

Christine A. Lekutis
Registration No. 51,934

MEDLEN & CARROLL, LLP
101 Howard Street, Suite 350
San Francisco, California 94105